

# **EFFECTS OF AN OPIOID AGONIST (U50,488H) AND ANTAGONIST (NALTREXONE) ON THE SEEKING AND INTAKE OF SUCROSE AND ETHANOL IN SELECTED AND NONSELECTED RATS**

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## **Abstract**

Naltrexone (NTX) is clinically efficacious at attenuating alcohol intake in non-abstinent alcoholics and, to a lesser extent, craving, independent of intake. While generally regarded as a nonselective opioid antagonist, NTX has been shown to have concentration dependent selectivity with lower doses (< 1.0 mg/kg) selective for the mu receptor and doses exceeding 1.0 mg/kg capable of binding to kappa receptors. While the mu system has been implicated in mediating the reinforcing effects of EtOH, the role of the kappa system is less clear. Recent evidence suggests that kappa activation may mediate EtOH aversion. Thus, the present study sought to evaluate the effects of the kappa agonist U50,488H (U50) in a paradigm that procedurally separates the motivation to seek vs. consume a reinforcer to assess whether U50 differentially affects these behaviors in both selected (alcohol-preferring P rats) and nonselected (Long Evans) rats, and whether these effects are specific to EtOH. The effects of a low (mu specific) and high (nonspecific) dose range of NTX were also assessed. Rats were trained to complete a single response requirement that resulted in access to either 2% sucrose or 10% EtOH for a 20-min drinking session. In three separate experiments, rats were injected (using a balanced design) with either saline or 1 of 3 doses of drug: U50 (IP; 2.5, 5.0, or 10.0mg/kg), low NTX (SC; 0.1, 0.3, or 1.0 mg/kg) or high NTX (SC; 1.0, 3.0, or 10.0 mg/kg) on both consummatory and appetitive treatment days. Following either a 15 (U50) or 30 minute (NTX) pretreatment, rats were placed into an operant chamber and intake (consummatory) or lever responses (appetitive) and response latencies were recorded. The results showed that overall, U50 and NTX attenuated intake and responding for sucrose and EtOH. Independent of reinforcer, LE rats were more sensitive to U50's effects on intake while P rats were more sensitive to the effects on seeking. P rats were more sensitive overall to lower doses of NTX than LE rats and lower doses of NTX were more selective in attenuating EtOH responding vs. sucrose. Higher doses of NTX suppressed intake and responding across both lines and reinforcers. These results demonstrate that craving and intake may be differentially regulated by the kappa and mu opioid receptor systems as a function of "family history" and suggest that different mechanisms of the same (opioid) system may differentially affect craving and intake. Supported by T32-AA007462